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Antimicrobial Stewardship Strategy: Intravenous to oral conversion

Promoting the use of oral antimicrobial agents instead of intravenous administration when clinically indicated.

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This is a PHO CORE strategy

Priority Level: **A**

Difficulty Level: **1**

Program Stage:

- ✓ Early
- Intermediate
- Advanced

Antimicrobial Stewardship Outcomes:

- Drug utilization outcomes
- Clinical outcomes

For more information on these criteria and how they were developed, please see the Antimicrobial Stewardship Strategy Criteria Reference Guide.

Description

This is an overview and not intended to be an all-inclusive summary. As a general principle, patients must be monitored by the health care team after changes to therapy resulting from recommendations made by the antimicrobial stewardship team.

Intravenous to oral conversion (IV to PO) involves a policy or guideline for switching the route of administration after careful patient assessment.

Rationale

This strategy has numerous benefits for patients and results in lower health care costs, so it is highly encouraged. Still, studies have shown that antimicrobials with high bioavailability are given intravenously to patients who could tolerate oral intake nearly 50 per cent of the time.[1]

Antimicrobials that have high bioavailability and are available in both intravenous and oral formulations (e.g., fluoroquinolones, linezolid, cotrimoxazole, fluconazole) are prime candidates for an IV to PO conversion program and should be given orally if the patient has a functioning gastrointestinal tract, because in such cases there is no advantage to IV administration.

Other antimicrobials can be switched to oral agents that have similar activity (e.g., cefazolin to cephalexin) when the patient's clinical condition has improved according to predefined criteria (e.g., afebrile, white blood cells normalizing, gastrointestinal tract functioning).

A switch to an oral agent can also occur in conjunction with de-escalation, based on susceptibility results (see De-escalation and streamlining).

Implementation

There are several ways to encourage the use of oral agents when possible:

- Policies and guidelines to switch to an appropriate oral agent automatically when certain criteria are met. These automatic substitution policies usually pertain to highly bioavailable agents.
- Transitioning to oral therapy may be performed in consultation with the prescriber when patients meet specific clinical parameters.
- Chart reminders may be used to remind the prescriber once a patient meets specific criteria.
- Many institutions have identified ways to flag patients who may be candidates for IV to PO conversion for review. This may include a manual review of patient profiles by clinical pharmacists via reports generated by pharmacy computer systems or clinical decision support systems.
- Pharmacy and therapeutics committee approval would be required for formalized and/or criteria-based programs if they are pharmacist or nurse-led.

Advantages

- Many potential benefits, including reductions in adverse effects related to the intravenous catheter (e.g., infection, thrombus formation), health care worker workload, patient length of stay, and hospital costs.[1,2]
- Most infectious-disease guidelines (e.g., community acquired pneumonia, skin and soft tissue infections, urinary tract infections, intra-abdominal infections, etc.) include recommendations for switching to oral antimicrobials once the patient has stabilized.
- IV to PO conversion programs may be initiated or performed by pharmacists or other health care workers based on predetermined clinical criteria.
- When done according to predetermined criteria, this strategy does not compromise patient outcomes.
- Preferential use of the oral route for antimicrobial agents with high bioavailability is a focus of the Association of Medical Microbiology and Infectious Disease Canada/Choosing Wisely Canada program recommendations.[3]

Disadvantages

- May encounter physician or nurse reluctance/reservations, even if criteria are met.
- Requires pharmacy (or other) staff to review antimicrobial orders and assess suitability for oral treatment.
- Could encourage unnecessarily prolonged courses of antimicrobials if the patient is switched to oral agents at or near completion of a treatment course and the stop date is inappropriately extended.

Requirements

- Staff to develop policy, procedures and/or guidelines for formalized programs/initiatives.
- Staff resources to perform conversion.
- Computer software or other methods of identifying patients on IV antimicrobials targeted for possible conversion.

Associated Metrics

- Drug costs, utilization and/or duration of intravenous therapy for targeted antimicrobials.
- Trends in the ratio of IV to PO antimicrobial use for targeted antimicrobials.
- Number of accepted/rejected recommendations for the IV to PO switch.

References

1. Goff DA, Bauer KA, Reed EE, Stevenson KB, Taylor JJ, West JE. Is the "low-hanging fruit" worth picking for antimicrobial stewardship programs? Clin Infect Dis. 2012;55(4):587–92. Available from: http://cid.oxfordjournals.org/content/55/4/587.long

2. Dellit TH, Owens RC, McGowan JE Jr, Gerding DN, Weinstein RA, Burke JP, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. Clin Infect Dis. 2007;44(2):159–77. Available from: http://cid.oxfordjournals.org/content/44/2/159.long

3. Choosing Wisely Canada/Association of Medical Microbiology and Infectious Disease Canada. Five things physicians and patients should question [Internet]. Toronto, ON: Choosing Wisely Canada; 2015 [updated 2015 Sep 4; cited 2015 Oct 30]. Available from: http://www.choosingwiselycanada.org/recommendations/medical-microbiology-and-infectious-disease/

Additional Useful References

Select articles to provide supplemental information and insight into the strategy described and/or examples of how the strategy was applied; not a comprehensive reference list. URLs are provided when materials are freely available on the Internet.

- Cunha BA. Oral antibiotic therapy of serious systemic infections. Med Clin North Am. 2006;90(6):1197–222.

- Kuper K. Intravenous to oral therapy conversion. In: Murdaugh LB. Competence assessment tools for health-system pharmacies. 4th ed. Bethesda, MD: American Society of Health-System Pharmacists; 2008. p. 347–60.
  Available from: http://shea-online.org/assets/files/other_papers/iv_to_po.pdf

  Excellent instructional paper outlining key considerations for use of oral drugs, including antimicrobials. (An updated chapter has been published but is not publically available).

- Béïque L, Zvonar R. Addressing concerns about changing the route of antimicrobial administration from intravenous to oral in adult inpatients. Can J Hosp Pharm. 2015;68(4):318–26.

- Barlow GD, Nathwani D. Sequential antibiotic therapy. Curr Opin Infect Dis. 2000;13(6):599–607.

  Reviews the principles of sequential (IV to PO) therapy and its application in selected infections.

- Dunn K, O'Reilly A, Silke B, Rogers T, Bergin C. Implementing a pharmacist-led sequential antimicrobial therapy strategy: a controlled before-and-after study. Int J Clin Pharm. 2011;33(2):208–14.

  Improved the timeliness of the IV to PO switch and decreased the duration of IV therapy with a pharmacist-led initiative using guidelines and clinical criteria to recommend changing route of administration.

- McLaughlin CM, Bodasing N, Boyter AC, Fenelon C, Fox JG, Seaton RA. Pharmacy-implemented guidelines on switching from intravenous to oral antibiotics: an intervention study. QJM. 2005;98(10):745–52. Available from: http://qjmed.oxfordjournals.org/content/98/10/745.long

  A pharmacist-led IV to PO program involving specific criteria and chart reminders that demonstrated reductions in IV antimicrobial use and costs.

Samples/Examples

- Example 1: Markham Stouffville Hospital Corporation - Pharmacist-initiated IV to PO Conversion Program of Antimicrobials
- Example 2: The Ottawa Hospital - Pharmacist-initiated Intravenous (IV) to Oral (PO) Automatic Substitution for Antimicrobial Agents
- Example 3: Alberta Health Services Antimicrobial Stewardship Backgrounder - Intravenous to Oral Antimicrobial Therapy Conversion

These documents have been generously shared by various health care institutions to help others develop and build their antimicrobial stewardship programs. We recommend crediting an institution when adopting a specific tool/form/pathway in its original form.

Examples that contain clinical or therapeutic recommendations may not necessarily be consistent with published guidelines, or be appropriate or directly applicable to other institutions. All examples should be considered in the context of the institution's population, setting and local antibiogram.

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Links with Other Strategies

- Checklists
- De-escalation and streamlining
- Disease-specific treatment guidelines, pathways, algorithms and/or associated order forms
- Prospective audit with intervention and feedback
- Scheduled antimicrobial reassessments ("antibiotic time outs")

Disclaimer

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For further information

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Example 1: Markham Stouffville Hospital Corporation - Pharmacist-initiated IV to PO Conversion Program of Antimicrobials

MARKHAM STOUFFVILLE HOSPITAL CORPORATION

INTERDISCIPLINARY MANUAL

AUTHOR:	Director of Pharmacy	**FOLDER:**	Medication Guidelines & Protocols
APPROVED BY:	DTC	**REVIEW FREQUENCY:**	3 years
RESPONSIBILITY:	Director of Pharmacy	**ORIGINAL APPROVAL DATE:**	14/11/02
POLICY HISTORY/ NUMBER CHANGES:		**REVISED/REVIEWED DATE:**	18/12/08 05/04/12

290.914.916.010 PHARMACIST-INITIATED IV TO PO CONVERSION PROGRAM OF ANTIMICROBIALS

POLICY:

Early conversion from intravenous (IV) to oral (PO) antimicrobials therapy is effective for a variety of infections. Many oral antimicrobials now have available excellent bioavailability. Conversion from IV to PO antimicrobials therapy in selected patients is an effective way of achieving cost savings for the Hospital (drug costs and nursing/pharmacy labour costs) while aiming for a positive clinical outcome. The switch to oral therapy must be individualized based upon the patient's clinical status and infection.

EXPECTED OUTCOME:

Pharmacists will monitor patients receiving IV antimicrobials, determine their eligibility for conversion to oral treatment, and initiate where appropriate the conversion from IV to PO therapy. The conversion will be documented in the patient's electronic record and on the Doctor's Orders sheets. All conversions will be followed to monitor clinical and pharmaco-economic outcomes. (See examples in **Appendix A - Suggested Antimicrobial Conversion Table**)

PROCEDURE/GUIDELINE:

The inclusion criteria for the pharmacist-initiated automatic conversion program include:

Example 1: Markham Stouffville Hospital Corporation - Pharmacist-initiated IV to PO Conversion Program of Antimicrobials (continued)

- The patient has received 48 hours of IV antimicrobials.
- The patient is improving clinically (i.e. afebrile for at least 24 hours, leukocytes normalizing, hemodynamically stable, and not septic).
- The patient has a functional GI tract, is able to take oral or NG nutrition and/or medications and there is no evidence of malabsorption.
- The pathogen is not known to be resistant to the antimicrobial to be used.
- The patient does not fall under the parameters of exclusion (see below)

Patients should NOT be switched to oral therapy if they meet any of the following exclusion criteria:

- The patient is being treated for an infection where parenteral therapy is indicated, such as Endocarditis, CNS infection (e.g. meningitis, encephalitis), *S aureus* or *Enterococcus* spp. Bacteremia.
- The patient may have an unreliable response to oral therapy due to continuous NG suction, malabsorption syndrome, ileus, protracted vomiting, severe diarrhea.
- The patient is ≤ 18 years (i.e. Pediatrics).

Example 1: Markham Stouffville Hospital Corporation - Pharmacist-initiated IV to PO Conversion Program of Antimicrobials (continued)

Appendix A - Suggested Antimicrobial Conversion Table

IV Drug	Oral Drug	Cost Savings/Day
Acyclovir 300 mg (5 mg/kg) q8h	Acyclovir 400 mg q8h **OR** Valacyclovir 500 mg q12h	$21.33 - $22.22
Ampicillin 1g q6h	Amoxicillin 500 mg q8h	$7.02
Azithromycin 500 mg q24h	Azithromycin 250 mg q24h	$18.67
Cefazolin 1g q8h	Cephalexin 500 mg q6h	$6.80
Cefuroxime 750 mg q8h	Cefuroxime Axetil 500 mg q12h	$9.84
Ceftazidime 2 g q6h	Ciprofloxacin 750 mg q12h	$21.39
Ceftriaxone 1 g q24h	Ciprofloxacin 500 mg q12h +/- Cephalexin 500 mg q6h	$4.91 -$5.49
Ciprofloxacin 400 mg q12h	Ciprofloxacin 500-750 mg q12h	$1.23 - $1.68
Clindamycin 600 mg q8h	Clindamycin 300 mg q6h	$8.65
Cloxacillin 1 g q6h	Cloxacillin 500 mg q6h	$14.86
Fluconazole 200 mg q24h	Fluconazole 200 mg q24h	$5.52
Gentamicin 300 mg (5 mg/kg) q24h	Ciprofloxacin 500 mg q12h **OR** Trimethoprim/Sulfamethoxazole (SEPTRA) 1 DS q12h	$9.78 $10.02
Meropenem 500 mg q6h	Ciprofloxacin 500-750 mg q12h + Metronidazole 500 mg q12h **OR** Ciprofloxacin 500-750 mg q12h + Clindamycin 300 mg q6h	$95.67 - $96.12 $94.71 - $95.16
Metronidazole 500 mg q12h	Metronidazole 500 mg q12h	$1.80
Moxifloxacin 400 mg q24h	Moxifloxacin 400 mg q24h	$31.02
Penicillin sodium 4 million units q6h	Penicillin VK 300 mg q6h	$8.89
Piperacillin/Tazobactam 4.5 g q8h	Amoxicillin/clavulanate 500/125 mg q8h **OR** Ciprofloxacin 500-750 mg q12h + Metronidazole 500 mg q12h **OR** Ciprofloxacin 500-750 mg q12h + Clindamycin 300 mg q6h	$26.02 $25.84 - $26.29 $24.88 - $25.33
Tobramycin 300 mg (5 mg/kg) q24h	Ciprofloxacin 750 mg q12h (for *Pseudomonas spp*)	$6.77
Trimethoprim/Sulfamethoxazole (SEPTRA) 10 mL q6h	Trimethoprim/Sulfamethoxazole (SEPTRA) 1 DS q12h	$47.76
Voriconazole 200 mg (4mg/kg) q12h	Voriconazole 200 mg q12h	$45.00

Example 2: The Ottawa Hospital - Pharmacist-initiated Intravenous (IV) to Oral (PO) Automatic Substitution for Antimicrobial Agents

October 3, 2013, version 2

PHARMACIST-INITIATED INTRAVENOUS (IV) TO ORAL (PO) AUTOMATIC SUBSTITUTION FOR ANTIMICROBIAL AGENTS

An automatic substitution policy has been endorsed by the Pharmacy and Therapeutics Committee and Medical Advisory Committee to authorize pharmacists at The Ottawa Hospital to change certain antimicrobials administered via the intravenous route to an oral route at an equivalent dose, provided the criteria outlined below are met.

This applies to adult patients prescribed the following agents.

Antimicrobial agent	F	Conversion ratio IV:PO	Examples	
			IV dose ⇨	Equivalent PO dose
Azithromycin	37%*	1:1	500 mg IV	500 mg PO
Ciprofloxacin**†	70-80%	1:1.25-1.88	400 mg IV	500-750 mg tablets PO**†
Fluconazole	>90%	1:1	200 mg IV	200 mg PO
Levofloxacin**	99%	1:1	750 mg IV	750 mg PO**
Linezolid	100%	1:1	600 mg IV	600 mg PO
Metronidazole	100%	1:1	500 mg IV	500 mg PO
Trimethoprim-sulfamethoxazole	90-100%	1:1	20 mL IV	2 DS tablets or 40 mL suspension PO

DS: double strength; F: bioavailability

*: azithromycin rapidly moves into tissues resulting in low serum concentrations, but high and persistent tissue concentrations, which makes it suitable for an IV to PO conversion.

**: ciprofloxacin should be administered at least 2 hours before or 6 hours after calcium, iron and other cations. Levofloxacin should be administered at least 2 hours before or 2 hours after these cations. Continuous enteral feeds should be held 1 hour before and after each dose of ciprofloxacin or levofloxacin.

† Do not administer via jejunostomy tube (J-tube) as it bypasses the main site of absorption. Do not use ciprofloxacin suspension with any tube as it may clog them.

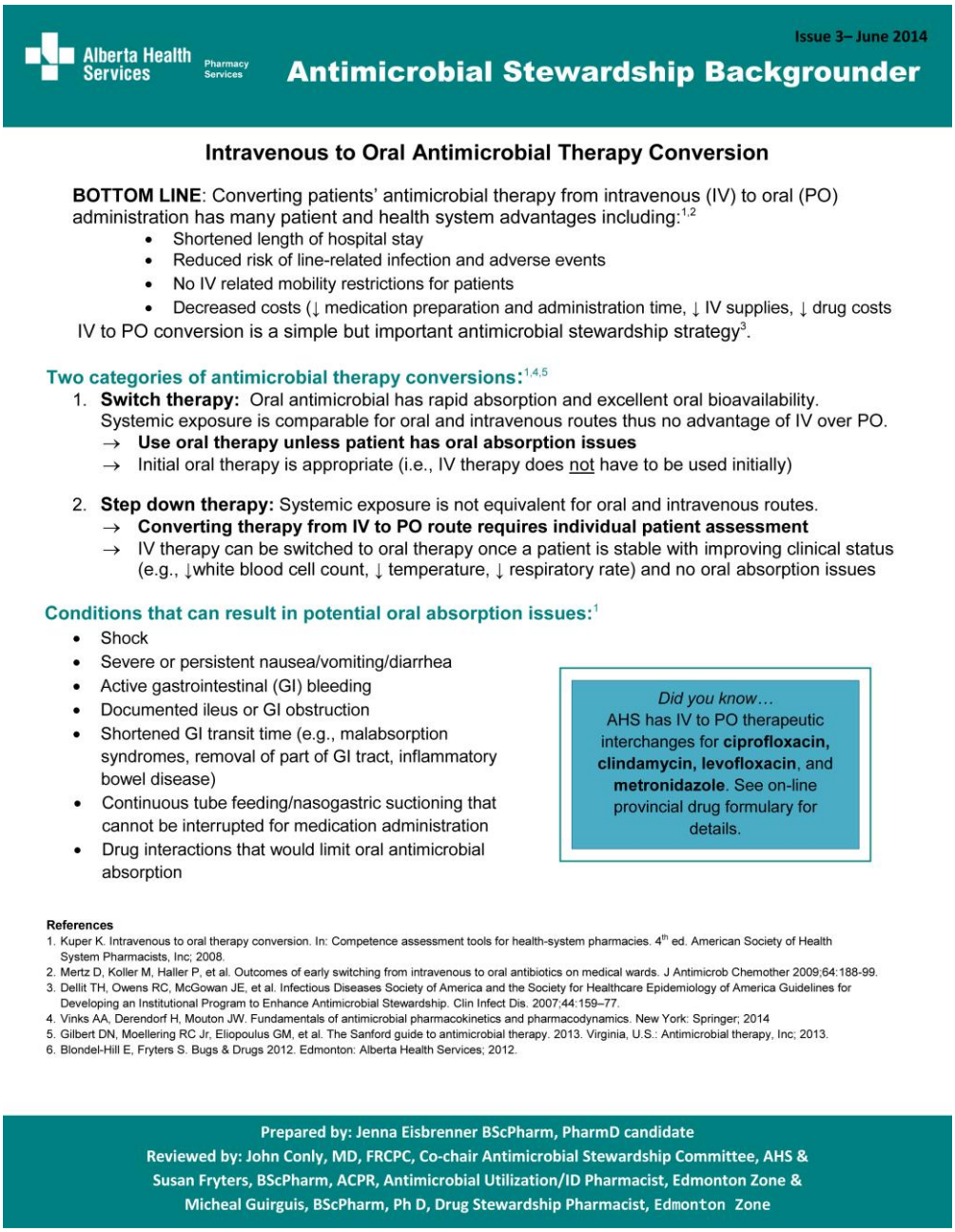
The antimicrobial agents listed above should be changed from IV to PO when all 3 of the following criteria are met and when patient's adherence to therapy is anticipated:

1) Improving clinically	2) Able to tolerate and absorb oral medications	3) No exclusion criteria
This may be indicated by: • Consistent improvement in fever over the last 24 hours or the patient is afebrile (<38°C) • White blood cells normalizing The patient should also be hemodynamically stable.	• Enterally fed or eating or drinking fluid diet, AND • Taking other medications orally, AND • No severe or persistent: nausea, vomiting or diarrhea, AND • No gastrointestinal obstruction, ileus, malabsorption syndrome, active gastrointestinal bleed, or continuous gastric suctioning	DO NOT change to PO if: • Meningitis, severe sepsis, endocarditis • Order for NPO in chart • Acute treatment phase of infections listed below (discuss with attending team or consult Infectious Diseases): – Osteomyelitis/discitis – Vertebral or deep abscesses – Bone and joint infections – Septic arthritis – Endophthalmitis • Patient admitted to Hem/BMT services

2. If the patient meets all of the above criteria and is receiving one of the designated antimicrobial agents, the pharmacist will write an order on a Physician's Order Form to have the IV form changed to an equivalent dose of the PO form. Orders will be prefaced by the phrase "MAC-approved IV to PO automatic substitution", followed by the specific order and the pharmacist's signature and printed name.

3. The pharmacist and the attending team will monitor the patient's clinical status and tolerability of the oral antimicrobial agent.

Example 3: Alberta Health Services Antimicrobial Stewardship Backgrounder - Intravenous to Oral Antimicrobial Therapy Conversion



Alberta Health Services | Pharmacy Services

Issue 3– June 2014

Antimicrobial Stewardship Backgrounder

Intravenous to Oral Antimicrobial Therapy Conversion

BOTTOM LINE: Converting patients' antimicrobial therapy from intravenous (IV) to oral (PO) administration has many patient and health system advantages including:[1,2]

- Shortened length of hospital stay
- Reduced risk of line-related infection and adverse events
- No IV related mobility restrictions for patients
- Decreased costs (↓ medication preparation and administration time, ↓ IV supplies, ↓ drug costs

IV to PO conversion is a simple but important antimicrobial stewardship strategy[3].

Two categories of antimicrobial therapy conversions:[1,4,5]

1. **Switch therapy:** Oral antimicrobial has rapid absorption and excellent oral bioavailability. Systemic exposure is comparable for oral and intravenous routes thus no advantage of IV over PO.
   → **Use oral therapy unless patient has oral absorption issues**
   → Initial oral therapy is appropriate (i.e., IV therapy does not have to be used initially)

2. **Step down therapy:** Systemic exposure is not equivalent for oral and intravenous routes.
   → **Converting therapy from IV to PO route requires individual patient assessment**
   → IV therapy can be switched to oral therapy once a patient is stable with improving clinical status (e.g., ↓white blood cell count, ↓ temperature, ↓ respiratory rate) and no oral absorption issues

Conditions that can result in potential oral absorption issues:[1]

- Shock
- Severe or persistent nausea/vomiting/diarrhea
- Active gastrointestinal (GI) bleeding
- Documented ileus or GI obstruction
- Shortened GI transit time (e.g., malabsorption syndromes, removal of part of GI tract, inflammatory bowel disease)
- Continuous tube feeding/nasogastric suctioning that cannot be interrupted for medication administration
- Drug interactions that would limit oral antimicrobial absorption

Did you know…
AHS has IV to PO therapeutic interchanges for **ciprofloxacin, clindamycin, levofloxacin**, and **metronidazole**. See on-line provincial drug formulary for details.

References

1. Kuper K. Intravenous to oral therapy conversion. In: Competence assessment tools for health-system pharmacies. 4th ed. American Society of Health System Pharmacists, Inc; 2008.
2. Mertz D, Koller M, Haller P, et al. Outcomes of early switching from intravenous to oral antibiotics on medical wards. J Antimicrob Chemother 2009;64:188-99.
3. Dellit TH, Owens RC, McGowan JE, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship. Clin Infect Dis. 2007;44:159–77.
4. Vinks AA, Derendorf H, Mouton JW. Fundamentals of antimicrobial pharmacokinetics and pharmacodynamics. New York: Springer; 2014
5. Gilbert DN, Moellering RC Jr, Eliopoulus GM, et al. The Sanford guide to antimicrobial therapy. 2013. Virginia, U.S.: Antimicrobial therapy, Inc; 2013.
6. Blondel-Hill E, Fryters S. Bugs & Drugs 2012. Edmonton: Alberta Health Services; 2012.

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Example 3: Alberta Health Services Antimicrobial Stewardship Backgrounder - Intravenous to Oral Antimicrobial Therapy Conversion (continued)

Alberta Health Services Pharmacy Services

Issue 3– June 2014

Antimicrobial Stewardship Backgrounder

IV to PO Conversion Recommendations[5,6]

Switch Therapy

Parenteral Therapy[α]	Cost ($)/Day[β]	Oral Therapy[α]	Cost ($)/Day[β]	Oral Bioavailability (%)
Ciprofloxacin 200-400 mg q12h	3.24 – 4.94	**Ciprofloxacin** 500-750 mg q12h	0.32 – 0.35	70
Clindamycin 600 mg q8h	25.59	**Clindamycin** 300-450 mg q6h	0.73 – 1.13	90
Fluconazole 400 mg daily	14.87	**Fluconazole** 400 mg daily	2.88	90
Levofloxacin 250-750 mg daily	4.98 – 13.59	**Levofloxacin** 250-750 mg daily	0.11 – 0.34	99
Linezolid 600 mg q12h	195.04	**Linezolid** 600 mg q12h	144.25	100
Metronidazole 500 mg q12h	3.38	**Metronidazole*** 500 mg q12h	0.25	100
Moxifloxacin 400 mg daily	17.51	**Moxifloxacin** 400 mg daily	4.00	89
Trimethoprim-sulfamethoxazole 160/800 mg q8h	38.60	**Trimethoprim-sulfamethoxazole** 1 DS tab q12h	0.21	85
Voriconazole 400 mg q12h x 2 doses then 200 mg q12h	571.80 285.90	**Voriconazole** 400 mg q12h x 2 doses then 200 mg q12h	41.54 20.77	96

* Excludes toxic megacolon.
α Usual adult dose with normal renal and hepatic function
β Inpatient drug costs. Parenteral therapy cost does not include the costs of IV administration or supplies

Step down Therapy[γ]

Parenteral Therapy[α]	Cost ($)/Day[β]	Oral Therapy[α]	Cost ($)/Day[β]	Oral Bioavailability (%)
Ampicillin 1-2 g q6h	18.00 – 36.00	**Amoxicillin** 500 mg q8h	0.19	80
Azithromycin 500 mg daily	8.32	**Azithromycin** 250 mg daily	0.64	37**
Cefazolin 1-2g q8h	2.33 – 4.65	**Cephalexin***** 500 mg q6h	0.46	90
Cefuroxime 0.75 – 1.5 g q8h	18.24 – 36.48	**Cefuroxime axetil** 0.5 – 1g q12h	1.84 – 3.68	52
Cloxacillin 1-2 g q6h	5.18 – 10.36	**Cephalexin** 500 mg q6h	0.46	90
Penicillin G 3-4 million units q6h	3.31 – 4.42	**Penicillin V** 300 mg q6h	0.18	60-73

** Low bioavailability but excellent distribution to tissues.
*** If a pathogen has been identified, ensure organism is susceptible to cephalexin.
α Usual adult dose with normal renal and hepatic function
β Inpatient drug costs. Parenteral therapy cost does not include the costs of IV administration or supplies.
γ Step down to oral therapy with these agents is not appropriate for certain infections due to severity or site of infection: endocarditis, meningitis, brain abscess, other central nervous system infections, orbital cellulitis, endophthalmitis and osteomyelitis[1].

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